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CASE SERIES

Indications and Four-Week Epithelialisation After Amniotic Membrane Transplantation for Ocular Surface Disorders in Padang, Indonesia: A Retrospective Case Series

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ABSTRACT

Background: Amniotic membrane transplantation (AMT) is widely used for ocular surface reconstruction, but no indication or outcome series from Sumatra, Indonesia, was found.

Objective: To describe the indications and four-week outcome of AMT at a tertiary referral hospital and compare them with published series.

Methods: Retrospective case series (STROBE) of all patients undergoing AMT at Dr. M. Djamil General Hospital, Padang, January 2022–December 2024. A favourable course was epithelialisation at four weeks without further surgery. Proportions carried Wilson 95% confidence intervals (CI) and were compared with published series using exact tests with Holm adjustment. Outcome was not linked to patient characteristics at eye level, so associations were bounded across all datasets consistent with the aggregate totals.

Result: Forty-three patients (47 eyes; 27 men, 62.8%) were included. Corneal ulcer was the leading indication (28 eyes, 59.6%; 95% CI 45.3–72.4), followed by grade IV pterygium and Stevens–Johnson syndrome-related symblepharon (each 14.9%). At four weeks, 40 eyes (85.1%; 95% CI 72.3–92.6) had a favourable course; six underwent repeat AMT and one, with Mooren's ulcer, evisceration. Keratitis formed a larger share of indications than in a Turkish audit (8.0%; Holm $p<0.001$). The available data could neither establish nor exclude an association of outcome with indication, sex or age.

Conclusion: At this Indonesian referral centre, AMT served chiefly as corneal reconstruction for ulcerative keratitis, and most eyes epithelialised within four weeks. Reoperation followed perforating corneal disease, immune-mediated melt and cicatrising SJS. Prospective eye-level registries are needed to identify predictors of failure.

1. Introduction

Corneal disease remains a major and largely avoidable cause of blindness in low- and middle-income countries. In a multicentre study of 15,937 inpatients with corneal disease in China, 58.2% had corneal blindness, keratitis caused 55.5% of it, and male sex and rural residence were independent risk factors.[1] Microbial keratitis drives much of this burden, and its aetiology is geographically patterned: fungi accounted for 57.2% of 3,581 culture-positive corneal scrapings in southern India and for 75.1% of cases in Nepal, whereas bacteria make up 44% of microbiologically confirmed keratitis worldwide.[2–4] Series from China, Vietnam and Malawi identify trauma, often agricultural, as a leading risk factor across tropical and subtropical settings.[5–7]

Indonesian data are sparse but consistent with this regional picture. A ten-year cohort of 1,100 eyes with corneal ulcer in Jakarta found that about two-thirds of patients were men, most were aged 41–60 years, trauma was the leading risk factor and infections were predominantly bacterial.[8] At a Jakarta tertiary eye centre, Gram-negative organisms made up 69.1% of bacterial isolates and *Pseudomonas aeruginosa* alone 36.2%.[9] Delay compounds severity: in Nepal more than half of patients with microbial keratitis presented at least seven days after symptom onset, and living more than 50 km from the eye hospital increased the odds of delay almost six-fold.[10] Patients who reach a referral centre after such delays frequently have deep, non-healing or perforating ulcers for which medical therapy alone is insufficient.

Amniotic membrane transplantation (AMT) is the most widely available surgical adjunct for these eyes. The membrane acts as a basement-membrane substitute and a reservoir of growth factors; its hepatocyte growth factor content depends on storage temperature, lyophilisation preserves its growth-factor load, and processed amnion suppresses inflammasome activity and shifts macrophages towards a reparative phenotype.[11–13] In infectious keratitis, a meta-analysis of 28 studies found that adjuvant AMT shortened time to healing by about four days and improved one-month visual acuity without excess adverse events.[14] Freeze-dried and cryopreserved membranes performed equivalently in corneal ulcers (89% vs 91% healed at three months).[15] Beyond keratitis, AMT is used for persistent epithelial defects, fornix reconstruction in Stevens–Johnson syndrome (SJS), pterygium excision and reconstruction after excision of ocular surface squamous neoplasia (OSSN).[16–19]

The success of AMT is nevertheless indication-dependent. Initial success after AMT for infectious keratitis ranged from 62.8% in a Spanish multicentre series to 66.7% in a Turkish series, falling to 53.3% in perforated eyes.[20,21] Four-week epithelial closure was 58.8% across 780 procedures for persistent epithelial defects in Germany, and repeat AMT was needed in 12.8% of eyes with severe ocular surface disorders in a 21-year Japanese series.[22,23] In refractory peripheral ulcerative keratitis (PUK), AMT combined with cryotherapy matched lamellar keratoplasty for primary healing but recurred more often, and spontaneous perforations frequently required more than one procedure.[24,25]

The mix of indications that brings patients to AMT also differs sharply between centres. Pterygium (42.7%) and symblepharon (27.0%) dominated in eastern Nepal, excision of ocular surface lesions (66.7%) in Türkiye, and a 12-year Italian tissue-bank

experience documented 5,349 membrane patches distributed for ocular surgery.[26–28] These differences reflect local disease, referral pathways and access to keratoplasty. Access to donor cornea is particularly constrained in Indonesia, where Lions Eye Bank Jakarta obtained only 47 local donors in eight years, so AMT is likely to carry a larger share of reconstructive and tectonic demand than in settings with ready keratoplasty.[29] A PubMed search in September 2026 combining amniotic membrane transplantation with Indonesia and Sumatra identified no series describing the indications for AMT, or its outcomes, from Sumatra.

This study therefore aimed to (1) describe the demographic profile, indications and corneal ulcer aetiology of patients undergoing AMT at a tertiary referral hospital in Padang, West Sumatra; (2) estimate the four-week clinical outcome with its precision; (3) compare the indication mix and outcomes quantitatively with published AMT and keratitis series; and (4) establish which associations between patient characteristics and outcome the available aggregate data could, and could not, identify.

2. Methods

Study design

This was a retrospective, single-centre case series with total sampling, conducted and reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guideline.

Ethical considerations

This study was approved by the Ethics Committee CMHC Indonesia (approval No. 336/2025). Because the study used anonymised hospital medical records, individual informed consent was waived. The study was conducted in accordance with the Declaration of Helsinki. No identifying information was extracted.

Setting and participants

The study was conducted at the Department of Ophthalmology, Dr. M. Djamil General Hospital, Padang, West Sumatra, Indonesia, a tertiary referral and teaching hospital affiliated with Universitas Andalas. All patients recorded as undergoing AMT between January 2022 and December 2024 were eligible. Inclusion required AMT performed within the study period and complete medical record data for the study variables. Patients with incomplete records, with follow-up shorter than four postoperative weeks, or who were lost to follow-up were excluded. An eye that reached an outcome event requiring further surgery before the fourth week was retained and classified by that event, because the event terminated follow-up rather than representing loss to follow-up. The number of patients excluded under each criterion was not documented; the flow of included patients is shown in Figure 1, and the potential influence of exclusions on the outcome estimate was examined by tipping-point analysis.

Variables and definitions

Variables were abstracted from the medical records: age in years, sex, laterality of AMT, indication, corneal ulcer aetiology, epithelialisation status at the four-week visit, and any further surgery. Age was analysed as reported and in ten-year bands. Indications were grouped as corneal ulcer, grade IV pterygium, SJS-related symblepharon, conjunctival neoplasia and persistent epithelial defect (PED), and further as corneal surface reconstruction (ulcer and PED) or conjunctival surface reconstruction (pterygium, symblepharon and neoplasia). Corneal ulcers were classified by the aetiology recorded in the chart as bacterial, fungal, mixed bacterial–fungal, viral or noninfectious; noninfectious ulcers included immune-mediated peripheral ulceration. Pterygium grade was taken from the clinical record; the grading system applied was not documented. Exposure keratopathy was not a separate category, and the bilateral patient with exposure keratopathy may have been recorded either as PED or as noninfectious ulcer, so analyses affected by this classification were run under both possibilities. Surgical technique (inlay, overlay or multilayer grafting; suture or glue fixation), the source and preservation of the membrane, microbiological confirmation method, ulcer size and depth, time from symptom onset to surgery and visual acuity were not documented consistently and were not analysed.

The primary outcome was the four-week clinical course. A favourable course was defined as complete epithelialisation at four weeks without the need for further surgery. An unfavourable course was defined as non-epithelialisation, recurrence (for symblepharon, re-adhesion) or progression (stromal melt, perforation or hypopyon) that led to further surgery, and was sub-classified by the procedure performed: repeat AMT or evisceration. Outcome status was taken from the clinical documentation of the four-week postoperative review. The outcome is therefore a surgery-driven composite: an SJS eye with recurrent adhesion may have had an epithelialised surface yet was classified as unfavourable because it required repeat surgery. Demographic proportions used the 43 patients as denominator; indications and outcomes used the 47 treated eyes.

Study size

Study size was fixed by the total number of eligible patients in the three-year window, and no a priori sample size calculation was performed. The precision attained was reported as the width of the 95% confidence interval at each key estimate, together with the number of eyes that would be required for a precision of ±10 and ±5 percentage points.

Statistical analysis

Univariate analysis. Every proportion was reported with a Wilson score 95% confidence interval, which retains nominal coverage at small sample sizes where the Wald interval does not. Exact binomial tests compared the sex ratio and the share of the leading indication with 50%, and the concentration of patients in the modal age band with a uniform distribution across bands; Cohen's h was reported as the effect size. The reported mean age was checked for consistency with the banded distribution by computing the range of means attainable from the band counts and the reported age range.

Comparison with published series. Comparator studies were identified through PubMed and selected according to four pre-specified rules: (i) an AMT indication audit, an AMT outcome series of at least 12 eyes, or a keratitis epidemiology study of at least 100 eyes or a meta-analysis; (ii) publication from 2021 onward, except that the two published AMT indication audits with comparable design (2016) were retained; (iii) a directly reported proportion for the same quantity; and (iv) where several studies qualified, the largest, with Indonesian or Asian studies preferred. Each proportion in this series was compared with its reference by a one-sample exact binomial test, with Cohen's h as the effect size, and the Holm procedure was applied across all 19 comparisons. Because one-sample tests treat the reference as a known constant, two-sample Fisher exact tests were added as a sensitivity analysis wherever the reference denominator was reported, using reference counts derived from the published percentage and denominator. A comparison was regarded as robust only if it remained significant after Holm adjustment and in the two-sample test. Outcome definitions and time points differed between series and are stated alongside each comparison.

Tipping-point analysis. Because the number of excluded patients was unknown, the number of additional patients with an unfavourable course that would have to be added to the denominator to remove each significant outcome comparison, or to reduce the favourable proportion to the benchmark value, was computed.

Bivariate analysis of observed joint distributions. Two joint distributions were observed. Sex by age band was tested

with the Fisher–Freeman–Halton exact test by complete enumeration of all 10,815 tables with the observed margins, with Cramér's V as effect size and the Cochran–Armitage test for trend in the female proportion across ordered bands (scores 0–6). Bilateral AMT by indication was tested at patient level with the Fisher–Freeman–Halton test under each of the two classifications possible for the bilateral patient with exposure keratopathy, and bilaterality in conjunctival versus corneal reconstruction with Fisher's exact test.

Bivariate sensitivity analysis over datasets consistent with the observed marginals. The four-week outcome was not cross-classified against sex, age or indication at eye level. Rather than impute a joint distribution, every eye-level contingency table consistent with the observed marginal totals was enumerated. Two scenarios were analysed. Scenario S0 used the margins alone, enumerating in addition every allocation of sex and age to the four bilateral patients. Scenario S1 additionally imposed the documented case-level facts for the eyes with an unfavourable course: no unfavourable course among pterygium or neoplasia eyes; two unfavourable SJS eyes (recurrent symblepharon); the eviscerated eye being a noninfectious ulcer in a man aged 41–50 years; and the remaining unfavourable eyes lying among corneal ulcer or PED eyes, with at most one PED eye. Because the diagnosis of each eye undergoing repeat AMT was not fully documented, only constraints consistent with six repeat AMT procedures and one evisceration were imposed, and every result that depends on S1 is conditional on these case-level facts. For each exposure and every admissible table, the odds ratio (OR, with Haldane–Anscombe correction for zero cells) and its 95% confidence interval, risk difference, Cramér's V or φ and Fisher's exact p were computed, and the attainable minimum and maximum of each measure and the percentage of admissible tables reaching $p<0.05$ were reported. For age as an ordinal exposure, the Cochran–Armitage statistic was computed across all admissible tables. An association whose attainable OR range spanned 1 was reported as one that the data could neither establish nor exclude; a direction that held in every admissible table was reported as consistent across the admissible space, and was interpreted in light of the number of eyes involved. When a scenario admitted only one or two tables, the percentage of significant tables was not interpreted.

Multivariable sensitivity analysis. The purpose of the multivariable analysis was to establish whether any adjusted association could be identified from the aggregate data, not to estimate adjusted effects, which seven events cannot support (2.3 events per variable). Firth-penalised logistic regression, which remains finite under the separation that small samples produce, was fitted for an unfavourable course with sex, age band (per ten-year step) and corneal ulcer indication as predictors. Admissible eye-level datasets were generated by permuting the observed sex–age pairs across patients, which preserves the observed sex by age table exactly, respecting the recorded diagnoses of the bilateral patients, and placing the seven unfavourable eyes subject to each scenario's constraints; 1,500 datasets were fitted per scenario. Hill-climbing searches that exchanged outcome labels between eyes, or sex–age pairs between patients, were then run towards the minimum and maximum of each coefficient (six restarts of 250 iterations per direction). Significance was assessed with penalised likelihood-ratio tests. For each predictor the attainable range, the 2.5th–97.5th percentile range and the percentage of datasets with $p<0.05$ were reported; the median across datasets is shown for orientation only.

Clustering. Four patients contributed two eyes. The proportion of patients with an entirely favourable course was bounded by the two possible allocations of the unfavourable SJS eyes to patients.

Analyses used Python 3.14 with SciPy 1.18, NumPy 2.4 and statsmodels 0.15; figures were produced with matplotlib 3.10. Random number generation used a fixed seed (20260914), and the analysis scripts are provided as supplementary material. Tests were two-sided with $\alpha=0.05$; p values are reported to three decimal places, and values below 0.001 from exact tests are reported as $p<0.001$. Multiplicity adjustment was applied to the benchmark family; the sensitivity analyses characterise the space of possible associations and are not confirmatory.

3. Results

Participants

Forty-three patients contributing 47 treated eyes met the eligibility criteria (Figure 1). Their characteristics are presented in Table 1 and Figure 2. The reported mean age was 41.8 years (range 2–70), which lies within the interval of means attainable from the banded distribution (40.3–48.9 years). The 41–50-year band was the largest, with 13 patients (30.2%; 95% CI 18.6–45.1), a concentration greater than expected under an even spread across the seven bands (exact binomial p=0.007; h=0.39). Five patients (11.6%; 95% CI 5.1–24.5) were aged 20 years or younger, three of them 10 years or younger. The standard deviation and median of age were not available.

Men accounted for 27 patients (62.8%; 95% CI 47.9–75.6) and women for 16 (37.2%; 95% CI 24.4–52.1); the sex ratio did not differ significantly from parity (p=0.126; h=0.26). The age distribution did not differ significantly between men and women (Fisher–Freeman–Halton p=0.119; Cramér's V=0.485), and there was no significant trend in the female proportion across age bands (Cochran–Armitage z=1.43, p=0.153).

Thirty-nine patients (90.7%; 95% CI 78.4–96.3) underwent unilateral AMT and four (9.3%; 95% CI 3.7–21.6) bilateral AMT, contributing eight eyes: two patients with SJS-related symblepharon, one with grade IV pterygium and one with exposure keratopathy.

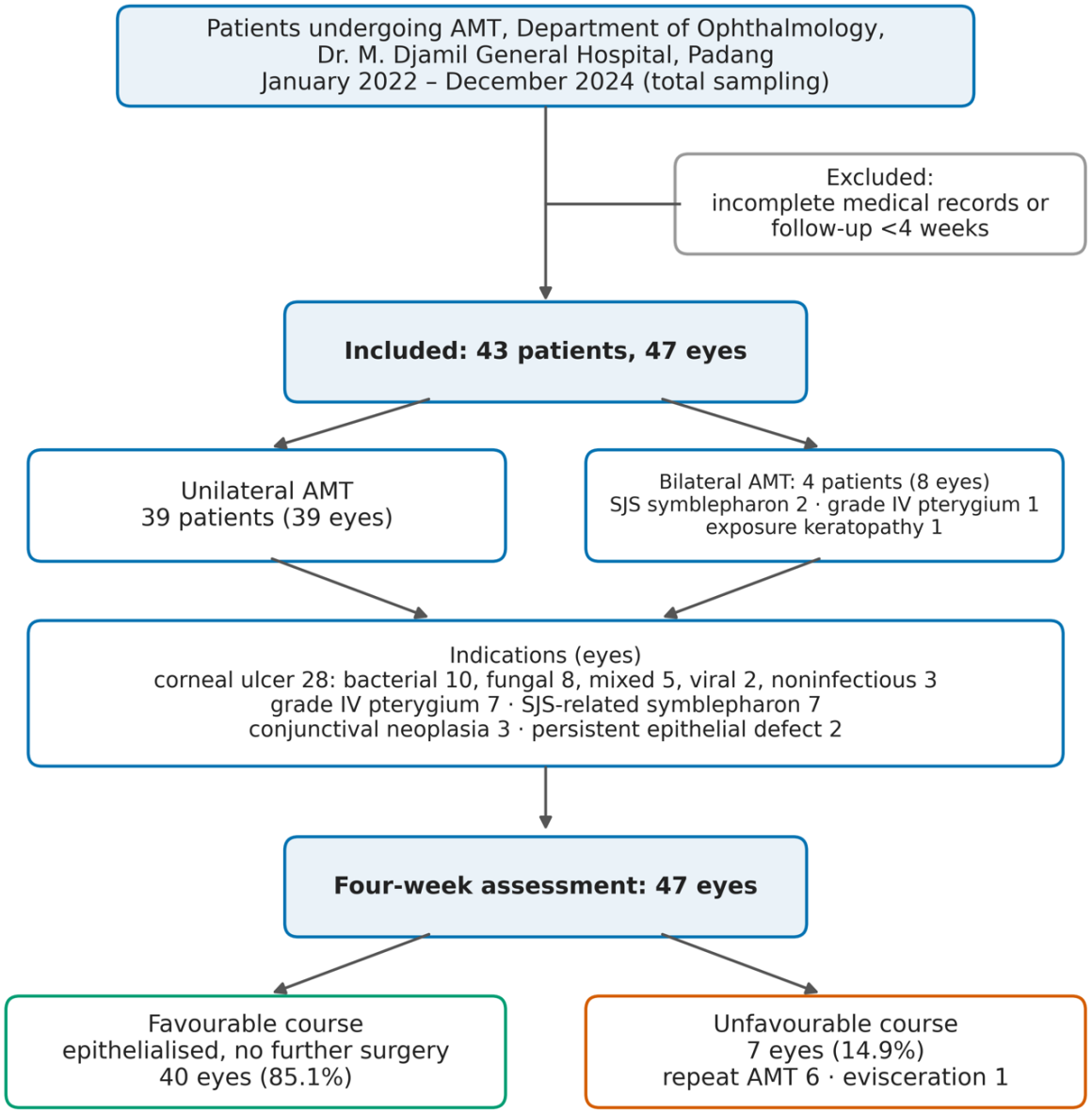

Figure 1. *Study flow diagram (STROBE). Patients who underwent amniotic membrane transplantation (AMT) at the Department of Ophthalmology, Dr. M. Djamil General Hospital, Padang, from January 2022 to December 2024, by laterality, indication and four-week outcome. SJS, Stevens–Johnson syndrome.*

Table 1. *Demographic characteristics of patients (n=43) and laterality of amniotic membrane transplantation*

Characteristic	Men, n (% of men)	Women, n (% of women)	Total, n (% [95% CI])
Age band, years	Age band, years	Age band, years	Age band, years
≤10	1 (3.7)	2 (12.5)	3 (7.0 [2.4–18.6])
11–20	2 (7.4)	0 (0.0)	2 (4.7 [1.3–15.5])
21–30	1 (3.7)	0 (0.0)	1 (2.3 [0.4–12.1])
31–40	7 (25.9)	1 (6.2)	8 (18.6 [9.7–32.6])
41–50	9 (33.3)	4 (25.0)	13 (30.2 [18.6–45.1])
51–60	5 (18.5)	3 (18.8)	8 (18.6 [9.7–32.6])
>60	2 (7.4)	6 (37.5)	8 (18.6 [9.7–32.6])
Total patients	27	16	43
Sex, % of 43 [95% CI]	62.8 [47.9–75.6]	37.2 [24.4–52.1]	—
Laterality of AMT	Laterality of AMT	Laterality of AMT	Laterality of AMT
Unilateral, patients	—	—	39 (90.7 [78.4–96.3])
Bilateral, patients (eyes)	—	—	4 (9.3 [3.7–21.6]); 8 eyes
Treated eyes	—	—	47

Confidence intervals are Wilson score intervals. Sex × age band (observed joint distribution): Fisher–Freeman–Halton exact p=0.119, Cramér's V=0.485; Cochran–Armitage trend for the female proportion across age bands z=1.43, p=0.153. Men vs parity: exact binomial p=0.126. Reported mean age 41.8 years (range 2–70). AMT, amniotic membrane transplantation.

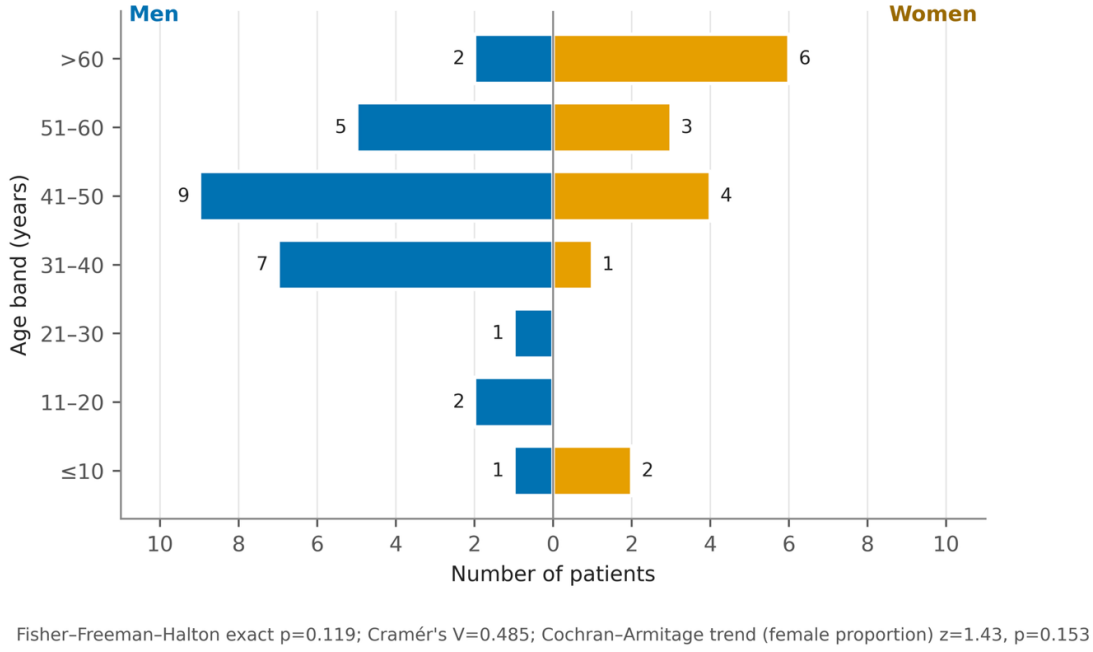

Figure 2. *Age and sex distribution of patients (n=43). Back-to-back bars show the observed number of men (left) and women (right) in each age band; the exact test statistics for the sex × age table are shown beneath the axis.*

Indications and corneal ulcer aetiology

Indications are presented in Table 2 and Figure 3. Corneal ulcer was the leading indication, accounting for 28 eyes (59.6%; 95% CI 45.3–72.4), more than the other four indications combined (19 eyes); its share did not, however, differ significantly from one half (p=0.243; h=0.19). Grade IV pterygium and SJS-related symblepharon each accounted for seven eyes (14.9%; 95% CI 7.4–27.7), conjunctival neoplasia for three (6.4%; 95% CI 2.2–17.2) and PED for two (4.3%; 95% CI 1.2–14.2). Corneal surface reconstruction accounted for 30 eyes (63.8%; 95% CI 49.5–76.0) and conjunctival surface reconstruction for 17 (36.2%; 95% CI 24.0–50.5).

Among the 28 ulcers, 10 were bacterial (35.7%; 95% CI 20.7–54.2), eight fungal (28.6%; 95% CI 15.3–47.1), five mixed bacterial–fungal (17.9%; 95% CI 7.9–35.6), two viral (7.1%; 95% CI 2.0–22.6) and three noninfectious (10.7%; 95% CI 3.7–27.2). An infectious aetiology was recorded in 25 ulcers (89.3%; 95% CI 72.8–96.3); bacteria were involved in 15 (53.6%) and fungi in 13 (46.4%).

Bilateral AMT was concentrated in conjunctival indications: three of 14 patients treated for conjunctival reconstruction and one of 29 treated for corneal reconstruction had bilateral surgery (Fisher p=0.094; OR 7.64, 95% CI 0.72–81.55). The test of bilateral surgery across the five indications depended on how the exposure keratopathy patient was classified (p=0.004 if classified as PED; p=0.113 if classified as noninfectious ulcer) and is therefore not interpreted.

Table 2. *Indications for amniotic membrane transplantation and corneal ulcer aetiology (n=47 eyes)*

Indication	Eyes, n	% of 47 eyes [95% CI]	Bilateral patients, n
Corneal surface reconstruction	30	63.8 [49.5–76.0]	
Corneal ulcer, all types	28	59.6 [45.3–72.4]	0 (1)[a]
Bacterial	10	21.3 [12.0–34.9]; of ulcers 35.7 [20.7–54.2]	
Fungal	8	17.0 [8.9–30.1]; of ulcers 28.6 [15.3–47.1]	
Mixed bacterial–fungal	5	10.6 [4.6–22.6]; of ulcers 17.9 [7.9–35.6]	
Viral	2	4.3 [1.2–14.2]; of ulcers 7.1 [2.0–22.6]	
Noninfectious	3	6.4 [2.2–17.2]; of ulcers 10.7 [3.7–27.2]	
Persistent epithelial defect	2	4.3 [1.2–14.2]	1 (0)[a]
Conjunctival surface reconstruction	17	36.2 [24.0–50.5]	
Grade IV pterygium	7	14.9 [7.4–27.7]	1
SJS-related symblepharon	7	14.9 [7.4–27.7]	2
Conjunctival neoplasia	3	6.4 [2.2–17.2]	0
Total	47	100.0	4

[a] *The bilateral patient with exposure keratopathy was classified in the record either as persistent epithelial defect or as noninfectious corneal ulcer; counts outside brackets assume the former, counts in brackets the latter. Corneal ulcer vs 50%: exact binomial p=0.243 (Cohen's h=0.19); corneal vs conjunctival reconstruction vs 50%: p=0.079. Bilateral AMT by indication (patient level): Fisher–Freeman–Halton p=0.004 (V=0.663) under the first classification and p=0.113 (V=0.417) under the second; conjunctival 3/14 vs corneal 1/29 patients, Fisher p=0.094, OR 7.64 (95% CI 0.72–81.55). SJS, Stevens–Johnson syndrome.*

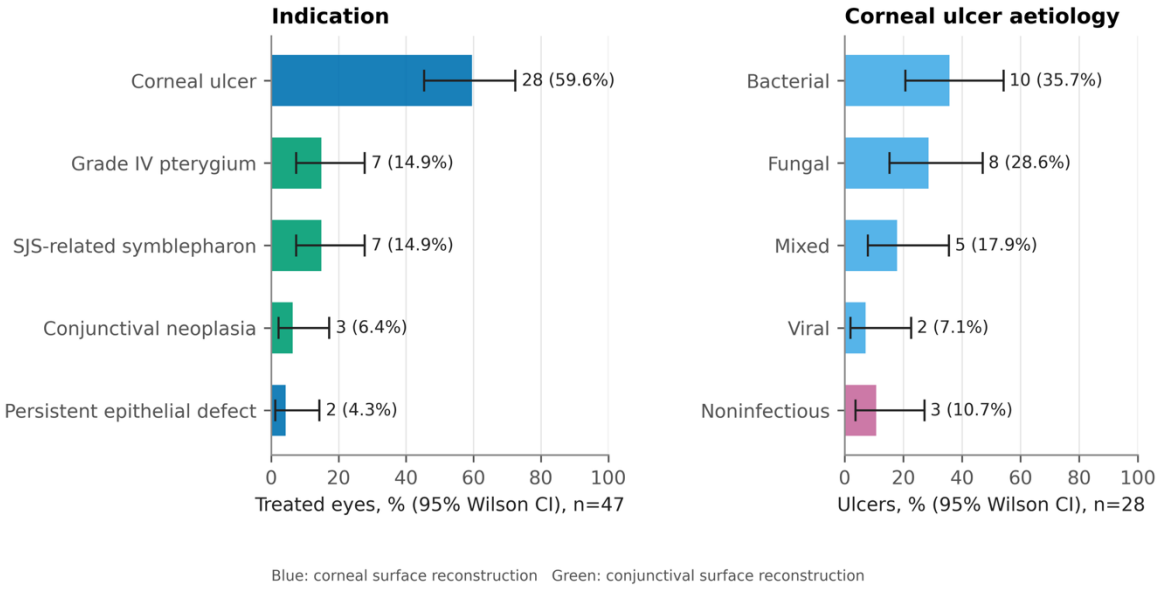

Figure 3. *Spectrum of indications for amniotic membrane transplantation. Left: indications as a proportion of 47 treated eyes (blue, corneal surface reconstruction; green, conjunctival surface reconstruction). Right: aetiology of the 28 corneal ulcers. Error bars are 95% Wilson confidence intervals. SJS, Stevens–Johnson syndrome.*

Four-week outcome

Four-week outcomes are presented in Table 3 and Figure 4. Forty eyes (85.1%; 95% CI 72.3–92.6) had epithelialised without further surgery. Seven eyes (14.9%; 95% CI 7.4–27.7) had an unfavourable course; six (12.8%; 95% CI 6.0–25.2) underwent repeat AMT and one (2.1%; 95% CI 0.4–11.1) evisceration. At patient level, between 36 (83.7%; 95% CI 70.0–91.9) and 37 (86.0%; 95% CI 72.7–93.4) of the 43 patients had an entirely favourable course, a band that contains the eye-level estimate.

Repeat procedures were performed for corneal disease with perforation or impending perforation, PUK and exposure keratopathy, and for recurrent symblepharon in two SJS eyes; no pterygium or neoplasia eye required further surgery. The eviscerated eye belonged to a 43-year-old man with Mooren's ulcer who developed a 3 mm hypopyon, progressive 360° peripheral corneal melt and perforation, and severe visual deterioration 14 days after AMT. Under these case-level facts (scenario S1), the unfavourable proportion was 14.3–17.9% among corneal ulcers, 0% among pterygium and neoplasia eyes, 28.6% (95% CI 8.2–64.1) among SJS eyes and 0–50% among PED eyes. The 95% confidence interval for the favourable course spanned 72.3–92.6% (width 20.3 percentage points); 49 eyes would be needed for a precision of ±10 points and 195 for ±5 points.

Table 3. *Four-week clinical outcome after amniotic membrane transplantation*

Outcome	n/N	% [95% CI]
Eye level (n=47)	Eye level (n=47)	Eye level (n=47)
Favourable course (epithelialised at 4 weeks, no further surgery)	40/47	85.1 [72.3–92.6]
Unfavourable course requiring further surgery	7/47	14.9 [7.4–27.7]
Repeat AMT	6/47	12.8 [6.0–25.2]
Evisceration	1/47	2.1 [0.4–11.1]
Within unfavourable course (n=7)	Within unfavourable course (n=7)	Within unfavourable course (n=7)
Repeat AMT	6/7	85.7 [48.7–97.4]
Evisceration	1/7	14.3 [2.6–51.3]
Patient level (n=43; bounds for bilateral patients)	Patient level (n=43; bounds for bilateral patients)	Patient level (n=43; bounds for bilateral patients)
All treated eyes favourable	36–37/43	83.7 [70.0–91.9] to 86.0 [72.7–93.4]
At least one unfavourable eye	6–7/43	14.0 [6.6–27.3] to 16.3 [8.1–30.0]
Unfavourable course by indication (scenario S1, case-level facts)	Unfavourable course by indication (scenario S1, case-level facts)	Unfavourable course by indication (scenario S1, case-level facts)
Corneal ulcer	4–5/28	14.3 [5.7–31.5] to 17.9 [7.9–35.6]
Grade IV pterygium	0/7	0.0 [0.0–35.4]
SJS-related symblepharon	2/7	28.6 [8.2–64.1]
Conjunctival neoplasia	0/3	0.0 [0.0–56.1]
Persistent epithelial defect	0–1/2	0.0 [0.0–65.8] to 50.0 [9.5–90.5]

Wilson score 95% confidence intervals. The unfavourable course comprised non-epithelialisation, recurrence or progression; the eviscerated eye (Mooren's ulcer) progressed 14 days after AMT. Patient-level bounds arise because two unfavourable SJS eyes may belong to one bilateral patient. Indication-specific rows derive from case-level clinical documentation and are partially identified: the corneal ulcer and PED rows depend on the classification of one repeat-AMT eye (exposure keratopathy); they are bounds, not observed cross-tabulations.

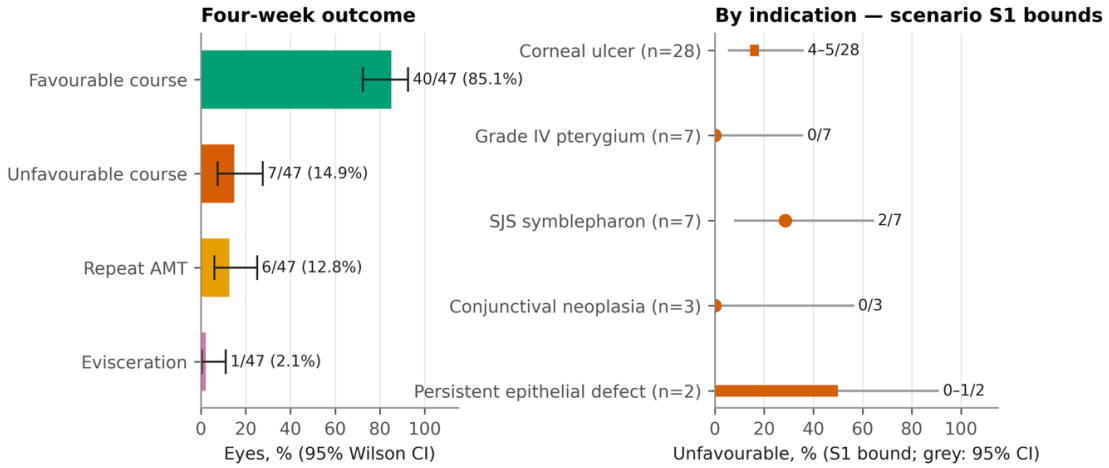

Figure 4. *Four-week clinical outcome. Left: favourable and unfavourable course and the additional surgery performed, as a proportion of 47 eyes with 95% Wilson confidence intervals. Right: unfavourable course by indication under scenario S1 (case-level facts); orange marks the attainable value or range and grey lines the envelope of 95% confidence intervals across that range. SJS, Stevens–Johnson syndrome.*

Comparison with published series

Comparisons are presented in Table 4 and Figure 5. Three of the 19 comparisons were robust to both Holm adjustment and the two-sample sensitivity test. Corneal ulcer formed a much larger share of indications than keratitis in a Turkish tertiary audit of 272 patients (59.6% vs 8.0%; Holm p<0.001; h=1.19; two-sample OR 16.75, 95% CI 8.09–34.67), and pterygium a much smaller share than in an audit of 211 eyes in eastern Nepal (14.9% vs 42.7%; Holm p<0.001; h=−0.63; OR 0.24, 95% CI 0.10–0.55). The shares of symblepharon (p=0.070) and PED (p=0.432) did not differ from those reference series. The proportion of men was similar to that of the Jakarta corneal ulcer cohort (p=0.628); the lower proportion than in the Nepalese audit (76.3%; unadjusted p=0.047) did not survive Holm adjustment (p=0.658).

The favourable four-week course (85.1%) exceeded four-week epithelial closure across 780 procedures for PED in Germany (58.8%; Holm p<0.001; h=0.60; two-sample OR 4.00, 95% CI 1.77–9.03). This comparison involves different populations: every eye in the German series had a persistent epithelial defect, whereas 36.2% of eyes in this series underwent conjunctival reconstruction. The difference would lose significance if nine excluded patients with an unfavourable course were added to the denominator, and the favourable proportion would fall to the German value only if 22 were added. The favourable course did not differ from single-AMT closure in a mixed Turkish series (74.2%; p=0.096). Among corneal ulcers, the favourable proportion (82.1–85.7% under S1) exceeded the Spanish post-keratitis benchmark of 62.8% in unadjusted one-sample tests (p=0.048 and p=0.011), but not after Holm adjustment (p=0.658 and p=0.176) or in two-sample tests against its 43 eyes (p=0.112 and p=0.058); comparisons with the Turkish keratitis series of 36 eyes were likewise not robust. Repeat-AMT (12.8%) and evisceration (2.1%) rates did not differ from Japanese, Nepalese, Turkish or North Sumatran reference figures in either test (all p≥0.174), and bacterial and fungal involvement among ulcers did not differ from global or South Asian proportions.

Table 4. *Comparison of indication mix, demography and outcomes with published amniotic membrane transplantation and keratitis series*

Quantity	This series, n/N (% [95% CI])	Reference %	Reference series	p (one-sample)	p (Holm)	Cohen's h	Two-sample sensitivity: reference n/N; OR [95% CI]; Fisher p
Corneal ulcer share of indications	28/47 (59.6 [45.3–72.4])	8.0	Tas 2024	<0.001	<0.001	+1.19	22/272; OR 16.75 [8.09–34.67]; p<0.001
Pterygium share of indications	7/47 (14.9 [7.4–27.7])	42.6	Hamal 2016	<0.001	<0.001	-0.63	90/211; OR 0.24 [0.10–0.55]; p<0.001
Symblepharon share of indications	7/47 (14.9 [7.4–27.7])	27.0	Hamal 2016	0.070	0.840	-0.30	57/211; OR 0.47 [0.20–1.12]; p=0.094
PED share of indications	2/47 (4.3 [1.2–14.2])	8.3	Tas 2024	0.432	1.000	-0.17	23/272; OR 0.48 [0.11–2.11]; p=0.554
Men (patients)	27/43 (62.8 [47.9–75.6])	66.7	Edwar 2026	0.628	1.000	-0.08	Reference n not reported
Men (patients)	27/43 (62.8 [47.9–75.6])	76.3	Hamal 2016	0.047	0.658	-0.30	Reference n not reported
Repeat AMT	6/47 (12.8 [6.0–25.2])	7.7	Harada 2025	0.174	1.000	+0.17	51/664; OR 1.76 [0.71–4.34]; p=0.258
Repeat surgery	6/47 (12.8 [6.0–25.2])	8.5	Hamal 2016	0.291	1.000	+0.14	18/211; OR 1.57 [0.59–4.20]; p=0.404
Repeat AMT	6/47 (12.8 [6.0–25.2])	14.5	Tas 2024	1.000	1.000	-0.05	39/272; OR 0.87 [0.35–2.20]; p=1.000
Favourable four-week course	40/47 (85.1 [72.3–92.6])	58.8	Süßmaier 2026	<0.001	<0.001	+0.60	459/780; OR 4.00 [1.77–9.03]; p<0.001
Favourable course (single AMT)	40/47 (85.1 [72.3–92.6])	74.2	Dikmetas 2024	0.096	1.000	+0.27	49/66; OR 1.98 [0.75–5.25]; p=0.243
Ulcer favourable course, S1 lower bound	23/28 (82.1 [64.4–92.1])	62.8	Lamas-Francis 2024	0.048	0.658	+0.44	27/43; OR 2.73 [0.86–8.59]; p=0.112
Ulcer favourable course, S1 upper bound	24/28 (85.7 [68.5–94.3])	62.8	Lamas-Francis 2024	0.011	0.176	+0.54	27/43; OR 3.56 [1.04–12.11]; p=0.058
Ulcer favourable course, S1 lower bound	23/28 (82.1 [64.4–92.1])	66.7	Subasi 2025	0.107	1.000	+0.36	24/36; OR 2.30 [0.70–7.56]; p=0.254
Ulcer favourable course, S1 upper bound	24/28 (85.7 [68.5–94.3])	66.7	Subasi 2025	0.043	0.645	+0.46	24/36; OR 3.00 [0.85–10.63]; p=0.144
Fungal involvement, ulcers	13/28 (46.4 [29.5–64.2])	57.2	Madduri 2024	0.258	1.000	-0.22	Reference n not reported
Bacterial involvement, ulcers	15/28 (53.6 [35.8–70.5])	44.0	Singh 2026	0.344	1.000	+0.19	Reference n not reported
Unfavourable course, SJS (S1)	2/7 (28.6 [8.2–64.1])	12.8	Harada 2025	0.223	1.000	+0.40	Reference n not reported
Evisceration	1/47 (2.1 [0.4–11.1])	2.8	Pardianto 2026	1.000	1.000	-0.04	13/467; OR 0.76 [0.10–5.94]; p=1.000

One-sample exact binomial tests treat the published proportion as fixed; Holm adjustment across all 19 comparisons. Two-sample Fisher exact tests use reference counts derived from the reported percentage and denominator. Corneal-ulcer rows are tested at the lower (23/28) and upper (24/28) bound of the favourable proportion under scenario S1. Reference series: Tas 2024 (Türkiye, 272 patients); Hamal 2016 (Nepal, 211 eyes); Edwar 2026 (Jakarta, 1,100 eyes); Harada 2025 (Japan, 664 eyes); Süßmaier 2026 (Germany, 780 procedures for persistent epithelial defect); Dikmetas 2024 (Türkiye, 66 eyes); Lamas-Francis 2024 (Spain, 43 eyes); Subasi 2025 (Türkiye, 36 eyes); Madduri 2024 (India, 3,581 isolates); Singh 2026 (global meta-analysis); Pardianto 2026 (Medan, Indonesia, 467 eyes). |h| ≥0.2 small, ≥0.5 medium, ≥0.8 large. PED, persistent epithelial defect; SJS, Stevens–Johnson syndrome.

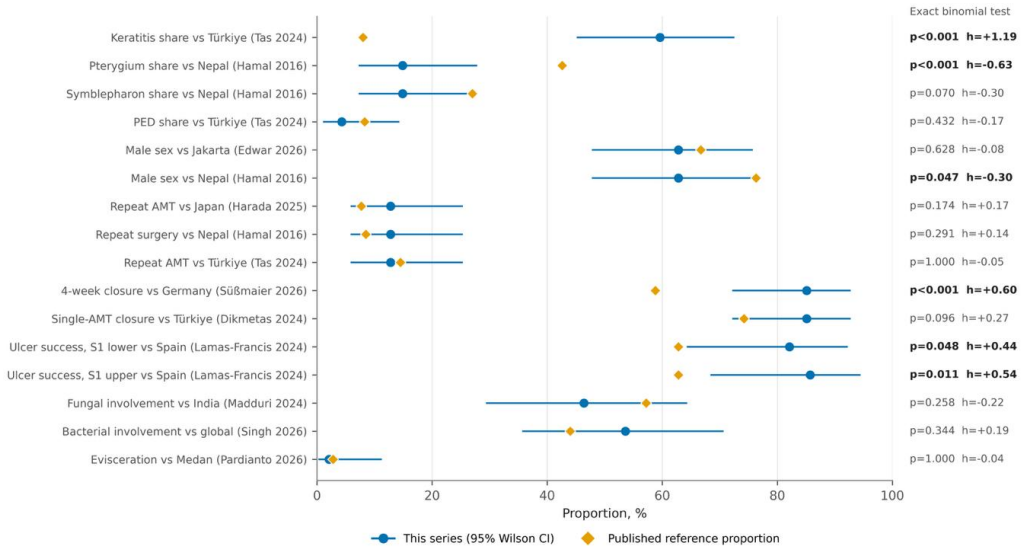

Figure 5. *Comparison with published series. Blue circles with bars show proportions in this series with 95% Wilson confidence intervals; orange diamonds show the reference proportion reported by each published series. Unadjusted one-sample exact binomial p values and Cohen's h are listed on the right, with bold text marking p<0.05; only the keratitis share, pterygium share and four-week comparison with the German series remain significant after Holm adjustment (Table 4). PED, persistent epithelial defect.*

Bivariate sensitivity analysis

The attainable ranges of association measures are presented in Table 5 and Figure 6. Under the margins alone (S0), the OR for an unfavourable course in corneal ulcers versus other indications ranged from 0.03 to 13.61 across eight admissible tables, three of which (37.5%) reached p<0.05; the corresponding ranges spanned the null for SJS symblepharon (0.30 to >100), conjunctival versus corneal reconstruction (0.09 to 43.57), male sex (0.02 to 15.00; 40 tables) and age older than 50 years (0.07 to 49.74). Across 198,652 admissible tables, the Cochran–Armitage statistic for age ranged from −5.62 to 3.88, and 29.3% of tables reached p<0.05. The marginal data could therefore neither establish nor exclude any outcome association.

Under the case-level facts (S1), the OR for corneal ulcers versus other indications narrowed to 0.89–1.85 in the two admissible tables (p 0.685–1.000), still spanning 1; the five-category indication test was non-significant in both admissible tables (p=0.296 and p=0.696). Sex, age and fungal involvement remained unidentifiable. Within corneal ulcers, noninfectious ulcers had a higher unfavourable proportion than infectious ulcers in all six admissible tables (OR 2.62 to >100; risk difference 17.3 to 96.0 percentage points), with significance in three of the six (p 0.001–0.459). This direction rests on three noninfectious ulcers and on the S1 case-level facts.

Table 5. *Bivariate sensitivity analysis over all contingency tables consistent with the observed marginals*

Exposure	Scenario	Admissible tables	OR (or V, z) range	Risk difference range, pp	Fisher p range	Tables p<0.05, %
Unfavourable course by exposure — attainable ranges across all admissible tables	Unfavourable course by exposure — attainable ranges across all admissible tables	Unfavourable course by exposure — attainable ranges across all admissible tables	Unfavourable course by exposure — attainable ranges across all admissible tables	Unfavourable course by exposure — attainable ranges across all admissible tables	Unfavourable course by exposure — attainable ranges across all admissible tables	Unfavourable course by exposure — attainable ranges across all admissible tables
Corneal ulcer vs other indications	S0	8	0.03 to 13.61	-36.8 to 25.0	0.001 to 1.000	37.5
	S1	2	0.89 to 1.85	-1.5 to 7.3	0.685 to 1.000	0.0
Conjunctival vs corneal reconstruction	S0	8	0.09 to 43.57	-23.3 to 41.2	<0.001 to 1.000	37.5
	S1	1	0.67 to 0.67	-4.9 to -4.9	1.000 to 1.000	0.0
SJS symblepharon vs other indications	S0	8	0.30 to >100	-17.5 to 100.0	<0.001 to 1.000	50.0
	S1	1	2.80 to 2.80	16.1 to 16.1	0.276 to 0.276	0.0
Male sex	S0	40	0.02 to 15.00	-43.8 to 25.9	<0.001 to 1.000	37.5
	S1	35	0.06 to 15.00	-34.3 to 25.9	0.004 to 1.000	28.6
Age >50 years	S0	40	0.07 to 49.74	-25.9 to 43.8	<0.001 to 1.000	37.5
Noninfectious vs infectious ulcer (28 ulcers)	S1	6	2.62 to >100	17.3 to 96.0	0.001 to 0.459	50.0
Fungal involvement vs other ulcers (28 ulcers)	S1	11	0.07 to 20.06	-33.3 to 38.5	0.013 to 1.000	27.3
Indication, five categories (Fisher–Freeman–Halton)	S0	226	V 0.15 to 1.00	—	<0.001 to 1.000	73.5
	S1	2	V 0.27 to 0.32	—	0.296 to 0.696	0.0
Age band, ordinal (Cochran–Armitage)	S0	198,652	z -5.62 to 3.88	—	<0.001 to 1.000	29.3
	S1	118,373	z -5.11 to 3.37	—	<0.001 to 1.000	25.0

Patient-level cross-classification of outcome against indication, sex or age was not available. S0 enumerates every eye-level table consistent with the published margins (including every allocation of the four bilateral patients' sex and age); S1 additionally imposes the case-level facts recorded for the unfavourable eyes (no unfavourable pterygium or neoplasia eye; two SJS recurrences; the eviscerated eye a noninfectious ulcer in a man aged 41–50; at most one unfavourable PED eye). An OR range spanning 1 indicates that the association cannot be identified from the data. OR with Haldane–Anscombe correction for zero cells. pp, percentage points; V, Cramér's V; z, Cochran–Armitage statistic.

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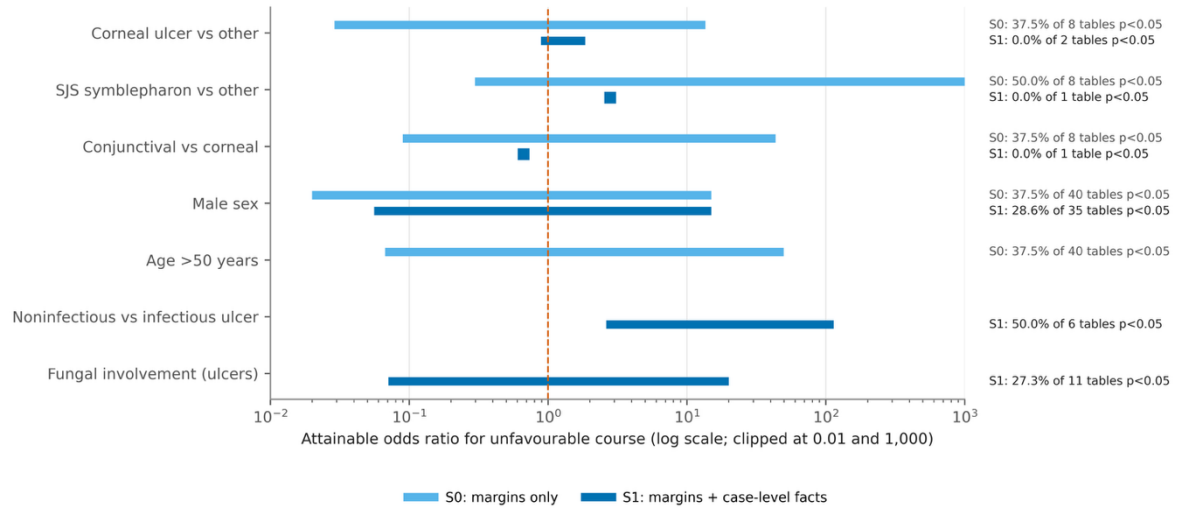

Figure 6. *Bivariate sensitivity analysis. Horizontal bars show the full range of odds ratios for an unfavourable course that is attainable across all contingency tables consistent with the observed marginals (S0, light blue) and with the additional case-level facts (S1, dark blue). The dashed line marks no association; a bar crossing it indicates that the association cannot be identified. The percentage of admissible tables reaching p<0.05 is shown on the right. SJS, Stevens–Johnson syndrome.*

Multivariable sensitivity analysis

Firth-penalised models are summarised in Table 6 and Figure 7. In both scenarios every predictor's attainable OR range spanned 1 by more than an order of magnitude. Male sex reached p<0.05 in 6.6% of datasets under S0 and 4.9% under S1, age band in 27.5% and 26.8%, and corneal ulcer indication in 4.5% and 0.0%. No adjusted association could be established or excluded.

Table 6. *Multivariable sensitivity analysis: Firth-penalised logistic regression for unfavourable course across admissible datasets*

Predictor	Median adjusted OR	2.5th–97.5th percentile	Attainable OR range	Datasets with p<0.05, %
Scenario S0 — margins only	Scenario S0 — margins only	Scenario S0 — margins only	Scenario S0 — margins only	Scenario S0 — margins only
Male sex	0.99	0.19–9.00	<0.01 to >100	6.6
Age band, per 10-year step	0.99	0.62–1.88	0.03 to >100	27.5
Corneal ulcer indication	0.94	0.20–5.50	<0.01 to >100	4.5
Scenario S1 — margins + case-level facts	Scenario S1 — margins + case-level facts	Scenario S1 — margins + case-level facts	Scenario S1 — margins + case-level facts	Scenario S1 — margins + case-level facts
Male sex	1.28	0.30–10.40	0.02 to >100	4.9
Age band, per 10-year step	1.01	0.67–1.91	0.15 to 9.77	26.8
Corneal ulcer indication	1.31	0.65–2.32	0.04 to >100	0.0

1,500 admissible eye-level datasets per scenario, generated by permuting the observed sex–age pairs across patients (preserving Table 1 exactly) and placing the seven unfavourable eyes subject to each scenario's constraints, plus hill-climbing searches towards each coefficient's minimum and maximum. p values from penalised likelihood-ratio tests. With seven events and three predictors (2.3 events per variable), these models bound what the data could show and do not estimate adjusted effects. OR, odds ratio.

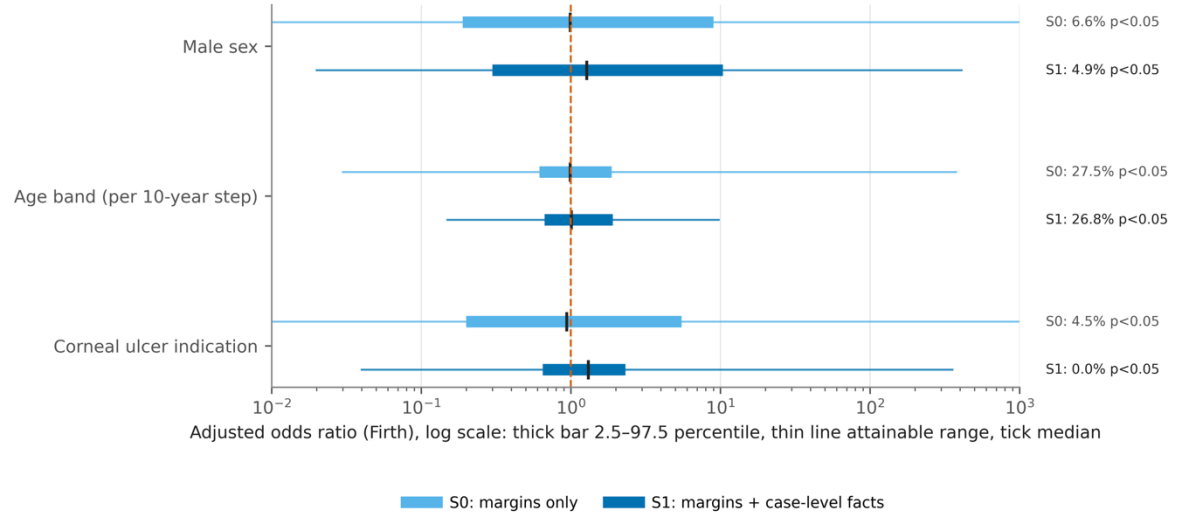

Figure 7. *Multivariable sensitivity analysis. Adjusted odds ratios from Firth-penalised logistic regression across 1,500 admissible datasets per scenario: thick bars span the 2.5th–97.5th percentiles, thin lines the attainable range after hill-climbing, and vertical ticks the median. Percentages give the share of datasets in which each predictor reached p<0.05.*

4. Discussion

Principal findings

This series describes 47 eyes of 43 patients treated with AMT over three years at Dr. M. Djamil General Hospital, Padang; no earlier AMT series from Sumatra was identified. Corneal ulcer, predominantly infectious, was the leading indication, and 85.1% of eyes had epithelialised without further surgery at four weeks. Every eye with an unfavourable course belonged to one of three disease processes — deep or perforating corneal disease, cicatrising SJS or immune-mediated peripheral melt — and the single globe loss followed Mooren's ulcer. The indication mix differed substantially and robustly from AMT audits in Nepal and Türkiye, while reoperation and evisceration rates were in line with published series. Whether outcome varies with indication, sex or age could be neither established nor excluded from the aggregate data, and the analysis quantified how wide that uncertainty is.

Indication mix in regional context

The dominance of corneal ulcer contrasts with the Nepalese audit, in which pterygium and symblepharon accounted for 69.7% of 211 eyes and the mean patient age was 28.1 years, and with the Turkish audit, in which keratitis accounted for 8.0% of 272 patients.[26,27] Outcome series from Japan, Korea and Türkiye likewise drew on a broad mix of ocular surface disorders rather than predominantly on infectious ulcers.[23,30,31] Three hypotheses, none testable with the present data, could explain the difference. First, microbial keratitis in tropical Asia is common, trauma-associated and frequently fungal, and the aetiological profile of ulcers in this series — bacterial involvement 53.6%, fungal involvement 46.4% — did not differ from global or South Asian proportions.[2,3,5] Second, a tertiary referral hospital receives ulcers after failure of primary treatment, and the delays documented in comparable health systems select for deep, non-healing ulcers.[7,10] Third, scarce donor cornea in Indonesia shifts tectonic and reconstructive work onto the membrane.[29] Occupation, trauma history, time to presentation and prior treatment were not captured, so none of these mechanisms can be attributed to the patients in this series.

The demographic profile resembled the Jakarta corneal ulcer cohort, with most patients in middle age and about two-thirds men.[8] The sex ratio did not differ significantly from parity, and no occupational data were available, so the frequently cited explanation that outdoor work exposes men to corneal trauma cannot be examined here. Male sex and rural residence were independent risk factors for corneal blindness in a Chinese multicentre study, which suggests that a larger sample might reveal a similar pattern.[1] Five patients were 20 years or younger. Young age features in two of the indications treated: age under 30 years was associated with severe chronic ocular complications of SJS in an international cohort, and infectious corneal perforation in children has been managed successfully with tenon patch grafting.[32,33] The diagnoses of the young patients in this series were not linked to their age in the records, so which indications they carried is unknown.

The Indonesian service context

The findings are best read against what is known about severe corneal disease in Indonesia. In Jakarta, a ten-year cohort of 1,100 ulcer eyes showed trauma as the leading risk factor and bacterial predominance, and a tertiary eye centre identified *Pseudomonas aeruginosa* as over a third of bacterial isolates.[8,9] In Medan, 467 eyes with descemetocele or iris prolapse were managed with cryotherapy over 17 years, preserving 97.2% of globes.[34] The volume of end-stage ulceration in these reports, the eight-year total of 47 local corneal donors at the Jakarta eye bank, and the predominance of ulcer among AMT indications in Padang together describe a system in which infectious keratitis reaches tertiary care late and keratoplasty is not readily available.[29] In such a system, the availability of amniotic membrane is itself a determinant of what surgery is possible. Dried and freeze-dried membranes perform comparably to cryopreserved membrane in corneal ulcers, and sutureless dehydrated membrane mounted on a contact lens healed all 23 eyes with acute chemical injury, so shelf-stable preparations are a practical option where cryopreserved tissue and a tissue bank are distant.[15,35] The source and preparation of the membranes used in Padang were not recorded, and documenting them should be part of any future audit.

Outcome definitions and comparability

Published AMT outcomes use different definitions and time points, which limits comparison. The German series reported epithelial closure at four weeks in eyes with persistent epithelial defects only; the Turkish mixed series reported closure after a single AMT; the Spanish and Turkish keratitis series defined success as healing without further surgery, with median or mean healing times of 40 and 21.7 days.[20–22,31] The outcome in this series was a surgery-driven composite at four weeks across corneal and conjunctival indications. The only outcome comparison that survived multiplicity adjustment and the two-sample test was with the German PED series, and it would lose significance had nine patients with an unfavourable course been among those excluded. Because 36.2% of eyes here underwent conjunctival reconstruction, in which epithelial failure is uncommon, this difference is likely to reflect case mix at least as much as the effectiveness of surgery. The favourable course among corneal ulcers was numerically higher than in the Spanish and Turkish keratitis series, but that difference was not robust.

Outcomes after AMT for corneal ulcer

The favourable four-week course among corneal ulcers, bounded at 82.1–85.7%, lies within the range of published results. Adjuvant cryopreserved overlay AMT gave a positive response in 76.9% of severe infectious ulcers, and initial success after AMT for infectious keratitis was 66.7% overall and 53.3% in perforated eyes, with repeat AMT needed in 46.7% of perforated eyes.[21,36] In refractory fungal ulcers, amniotic membrane grafting achieved 86.7% epithelialisation against 73.3% with a conjunctival flap, multilayer fresh AMT resolved or markedly improved 91.7% of treatment-resistant ulcers, and debulking biopsy with tectonic AMT resolved all 12 presumed fungal infections treated.[37–39] Multilayer AMT combined with a conjunctival flap healed all 16 small fungal perforations with preservation of every globe.[40] The meta-analytic estimate of a four-day reduction in healing time indicates a modest but consistent adjunctive effect in infectious keratitis.[14]

A four-week horizon captures early epithelialisation and early failure but not late recurrence, scarring or visual outcome, so some eyes classified as favourable may still have failed. The rate may also reflect case selection: eyes with large perforations may have gone directly to keratoplasty or evisceration, and patients lost before four weeks were excluded. Where perforation occurs, AMT plugging achieved 87.5% disease control in perforations smaller than 3 mm, comparable to lamellar keratoplasty with acellular porcine stroma, and tenon patch grafting healed 92.3% of 3–5 mm infectious perforations in children.[33,41] Tissue adhesive is an alternative, but a third of glued eyes progressed to penetrating keratoplasty, particularly after neurotrophic disease, and final visual acuity did not differ between glue alone and keratoplasty.[42,43] Spontaneous perforations required more than one procedure in 38.9% of eyes, and descemetocele, most often caused by microbial keratitis, achieved therapeutic success in only about half.[25,44] The evisceration rate of 2.1% is in keeping with the 2.8% reported from Medan, whereas endophthalmitis secondary to keratitis led to evisceration in 13.3% of eyes, underlining the importance of controlling infection before the globe is compromised.[34,45]

Mooren's ulcer, PUK and noninfectious ulceration

The eviscerated eye illustrates the principal limit of AMT (Figure 8, a proposed framework). Mooren's ulcer was the leading cause of PUK in a ten-year Thai cohort, in which

perforation occurred in 11.6% of eyes.[46] In a Chinese cohort of 101 eyes, perforation occurred in 18.8% and recurrence after keratoplasty in 37.3%, predicted by ulcer depth, perforation and prior surgery or trauma.[47] Among Black African patients with perforated Mooren's ulcer, 55.6% of eyes were blind and a third recurred.[48] In refractory PUK, AMT with cryotherapy healed as often as lamellar keratoplasty but recurred three times as frequently (32.1% vs 10.0%), and autoimmune disease prolonged epithelialisation.[24] The membrane supports epithelial closure and dampens local inflammation but cannot supply tectonic strength against an active immune melt; such eyes need systemic immunosuppression, close early review and a low threshold for tectonic surgery.

Noninfectious ulcers were a small category — three eyes — yet they carry the only consistent directional signal in the sensitivity analysis: under the S1 case-level facts, their unfavourable proportion exceeded that of infectious ulcers in every admissible table. This signal is conditional on those facts, rests on three eyes and reached significance in only half the admissible tables, so it is a hypothesis for prospective testing rather than a finding. Exposure keratopathy raises a related classification problem. It was not a separate category, the bilateral patient with exposure keratopathy may have been counted either as PED or as noninfectious ulcer, and the test of bilaterality by indication changed from p=0.004 to p=0.113 with that single decision. Exposure-related defects respond differently from infectious or immune-mediated ulcers: in a Saudi comparison, eyes treated with tarsorrhaphy had more baseline exposure keratopathy (40% vs 2.7%) than AMT-treated eyes, and in the United Kingdom, tarsorrhaphy was required in most eyes managed conventionally for persistent defects.[49,50] Future audits should record exposure keratopathy, neurotrophic keratopathy and immune-mediated ulceration as distinct indications.

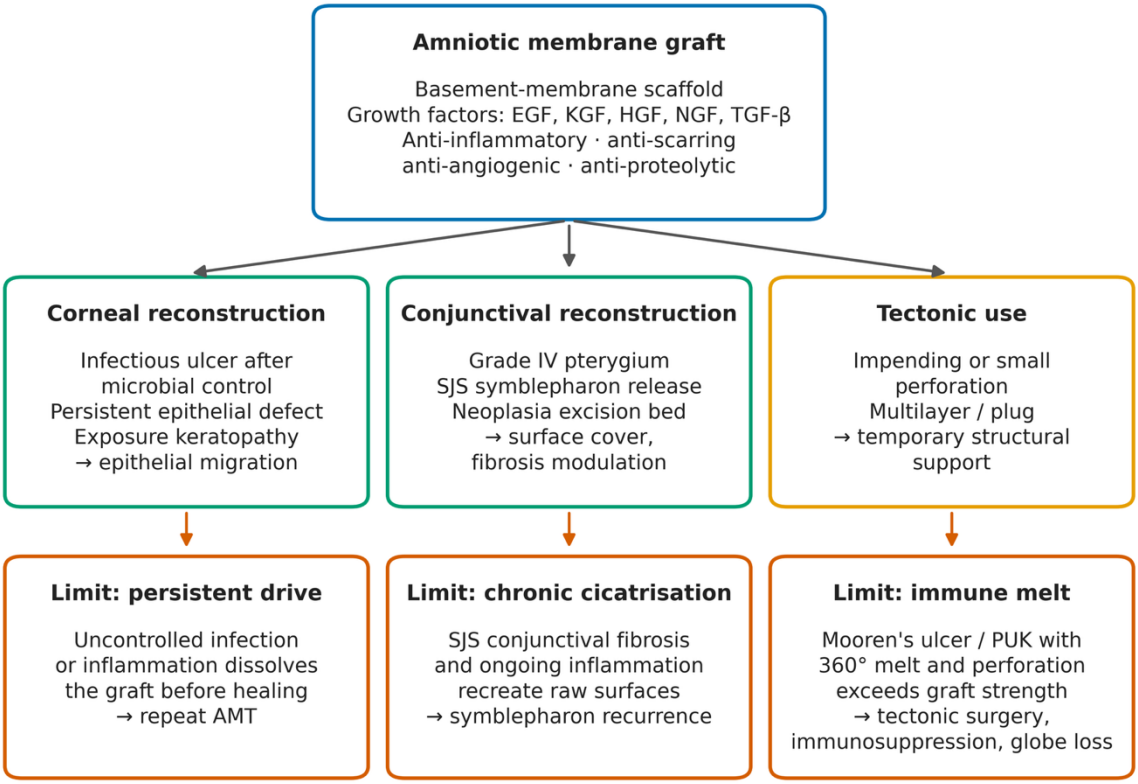

Figure 8. *Proposed framework linking the biological actions of the amniotic membrane to its three roles in this series (corneal reconstruction, conjunctival reconstruction, temporary tectonic support) and to the disease processes that limit each role. PUK, peripheral ulcerative keratitis; SJS, Stevens–Johnson syndrome.*

Recurrence in SJS-related symblepharon

Two of the seven SJS eyes (28.6%) required repeat AMT for recurrent symblepharon, higher than the 12.8% repeat-AMT rate in severe ocular surface disorders in Japan but compatible with it given the width of the interval.[23] Chronic ocular SJS is a persistent inflammatory and cicatrising disease rather than a single anatomical defect. Symblepharon was present in 47.5% of chronically affected eyes in a Hungarian cohort, and severe chronic ocular complications in an international cohort of 682 patients were associated with severe pseudomembranous conjunctivitis in the acute phase.[32,51] Surgical division of adhesions recreates opposing raw surfaces on a conjunctiva that remains inflamed, so re-adhesion is expected. Fornix reconstruction with AMT alone or combined with mitomycin C, oral mucosal grafts or limbal autografts succeeded in 88.8% of cases, and all three failures were symblepharon recurrences.[52] AMT is most effective when applied early: a systematic review of 54 studies found good visual outcomes and few chronic sequelae after AMT within two weeks of onset, and sutureless bedside AMT in the acute phase left no eye with symblepharon at six months, although five of 13 patients needed a second application.[17,53] Symblepharon formation was more frequent with cryopreserved AMT rings than with dehydrated AMT plus a symblepharon ring in a burn-unit series.[54] Patients with chronic SJS should therefore be counselled that a single AMT may not be curative, and referral pathways that bring acute SJS to ophthalmic care within the first two weeks may prevent the chronic disease seen here.

Pterygium, neoplasia and persistent epithelial defects

No pterygium, neoplasia or PED eye had an unfavourable course by four weeks, but four weeks cannot capture the failure modes that matter for these indications; the published comparisons below provide context for longer follow-up rather than a test of the present results. Pterygium recurrence typically becomes evident after several months. A meta-analysis of randomised trials found no significant difference in recurrence between AMT and conjunctival autograft, whereas autograft with mitomycin C reduced recurrence; for recurrent pterygium, AMT alone recurred in 80% of eyes against 17.7% with autograft.[18,55] A randomised trial found no difference in recurrence grade at 12

months between autograft and AMT with interferon, combined autograft and AMT after extended removal recurred in only 1.05% of 666 eyes, and recurrence across ten years of surgery in the Philippines was 1%.[56–58] Recurrence was more common in patients younger than 40 years.[59] Pterygium prevalence rises with lifetime ultraviolet exposure, and incidental OSSN is found in 1.32% of excised pterygia, more often at higher ultraviolet exposure — relevant at Padang's equatorial latitude, and a reason to submit excised grade IV pterygia for histology.[60,61] After OSSN excision with surface reconstruction, recurrence was 27.1%, predicted by tumour size and absence of adjuvant chemotherapy; lesion area predicted carcinoma in situ and squamous cell carcinoma in South India, and recurrence-free survival was 87.0% at one to three years in Hong Kong.[19,62,63] Squamous cell carcinoma recurred in 30.1% of cases in a Japanese tertiary series.[64] The histology of the three neoplasia cases in this series was not available. For PED, a single sutureless membrane resolved 45.5% of defects, AMT healed 86% of refractory defects against 70% after tarsorrhaphy, and graft failure in neurotrophic keratitis was predicted by systemic immunosuppression and repeated grafting.[16,49,65]

What the available data can and cannot show

Outcome was available as marginal totals, without linkage to patient characteristics for each eye. The sensitivity analysis converts this limitation into a quantified statement of what can and cannot be concluded. Under the totals alone, the possible association between indication and outcome ranged from a strong protective to a strong harmful effect; under the case-level facts it narrowed to an OR of 0.89–1.85, still spanning no difference. The data therefore do not show that outcome is independent of indication, sex, age or fungal aetiology; they show that no conclusion in either direction is possible. Adjusted models were uninformative, as expected with seven events. Eye-level linkage of outcome to indication, sex and age would convert every bound in Table 5 into an observed estimate.

Implications for comparable referral settings

The findings are from a single centre and apply most directly to tertiary referral hospitals with similar case mix and limited keratoplasty access. In such settings, AMT can be offered with an expectation of early epithelialisation across the common indications, provided the underlying infection is controlled, while recognising that the four-week result does not guarantee durable success. Eyes with immune-mediated peripheral melt or impending perforation require early escalation to systemic immunosuppression and tectonic surgery, and patients with chronic SJS should be counselled that repeat surgery is common. At system level, the reliance on AMT for corneal reconstruction argues for secure local supply of processed membrane, for donor cornea procurement and for earlier referral of keratitis.

Research agenda

Four studies would address the questions this series cannot answer. First, a prospective multicentre registry of AMT across Indonesian referral centres should record, for each eye, indication (with exposure, neurotrophic and immune-mediated ulceration as separate categories), microbiology, ulcer size and depth, perforation status, technique, membrane preparation, time from onset to surgery, time to epithelialisation, visual acuity, and outcomes at four weeks and at three, six and twelve months. With an unfavourable-course rate near 15%, about 336 eyes would provide the 50 events needed for a five-predictor model with ten events per variable. Second, within that registry, comparing unfavourable course between noninfectious and infectious ulcers, assuming 50% vs 15%, requires 27 eyes per group at 80% power and two-sided α=0.05; comparing SJS symblepharon with other indications at 28.6% vs 12.5% requires 96 per group. Third, a comparison of perforated with non-perforated ulcers, assuming repeat-AMT rates of 46.7% and 19.0% as reported in a Turkish series, requires 44 eyes per group.[21] Fourth, a pragmatic randomised trial of adjuvant AMT versus standard medical therapy in severe infectious keratitis would test whether the adjunctive effect shown in the meta-analysis holds in a setting of late presentation; detecting an improvement in healing without further surgery from 63% to 85% would require 59 eyes per arm.[14,20] Pterygium and neoplasia cohorts should be followed for at least 12 months with histology of every excised specimen.

Strengths and limitations

This study included every eligible patient treated with AMT over three years at a tertiary referral centre. It reported every estimate with an interval, compared its findings with published series under pre-specified selection rules, multiplicity adjustment and two-sample sensitivity tests, and analysed the full space of possible associations rather than asserting associations the data cannot support.

Several limitations apply. The design was retrospective, single-centre and small, with seven outcome events. Outcome was not linked to patient characteristics for each eye, so no association with outcome could be estimated directly. The diagnosis of each eye undergoing repeat AMT was not fully documented, and the classification of the exposure keratopathy patient is uncertain; scenario S1 is conditional on the documented case-level facts. Surgical technique, membrane source and preparation, the pterygium grading system, neoplasia histology, ulcer size and depth, microbiological confirmation, time to presentation, visual acuity, the dispersion of age and follow-up beyond four weeks were not available. The number of excluded patients was unknown, and the tipping-point analysis shows that the only significant outcome comparison would be lost with nine excluded failures. Benchmark comparisons involved different populations, outcome definitions and time points.

5. Conclusion

At a tertiary referral hospital in West Sumatra, AMT was used predominantly for corneal reconstruction in infectious ulcers, which made up 59.6% of treated eyes — a far larger share than in AMT audits from Nepal and Türkiye. Within four weeks, 85.1% (95% CI 72.3–92.6) of eyes had epithelialised without further surgery. Reoperation followed deep or perforating corneal disease and cicatrising SJS, and the only globe loss followed Mooren's ulcer. The aggregate data could neither establish nor exclude differences in outcome by indication, sex or age.

AMT should be combined with prompt control of infection and, for immune-mediated melt, early systemic immunosuppression and tectonic surgery, and patients with chronic SJS should be counselled that repeat surgery is common. A prospective multicentre Indonesian registry that records indication, technique, membrane preparation and outcomes for each eye beyond four weeks, powered to compare noninfectious with infectious ulcers, is the next step required to identify predictors of failure.

Ethics approval and consent to participate: This study was approved by the Ethics Committee CMHC Research Center, Indonesia (approval No. 336/2025). Because the study used anonymised hospital medical records, individual informed consent was waived. The study was conducted in accordance with the Declaration of Helsinki.

Consent for publication: Not applicable; no identifiable patient information or images are included.

Availability of data and materials: Aggregate data are reported in the article. Analysis scripts are provided as supplementary material. Patient-level data are not publicly available because of patient confidentiality.

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